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Office of Research Integrity

NEWSLETTER

The *ORI Newsletter* is published quarterly by the Office of Research Integrity, Office of the Secretary of Health and Human Services, and distributed to applicant or awardee institutions and PHS agencies to facilitate pursuit of a common interest in handling allegations of misconduct and promoting integrity in PHS-supported research. Please duplicate and circulate this newsletter freely. An electronic copy is available on the ORI home page.

IN THIS ISSUE

Association for Practical and Professional Ethics Hold Workshop in Response to NIH and NSF Requirements

James DuBois, Ph.D., D.Sc., Hubert Mäder Chair of Health Care Ethics, and Holly Bante, Ph.D. Candidate, M.P.H., M.S., Graduate Research Assistant, Albert Gnaegi Center for Health Care Ethics, Saint Louis University

At the 20th anniversary meeting on March 3-6, 2011, of the Association for Practical and Professional Ethics (APPE), the Responsible Conduct of Research Education Committee (RCREC) held a full-day workshop on "The Challenge of Research Ethics Education in the University Setting: A Response to NIH and NSF Requirements." Nearly 100 responsible conduct of research (RCR) instructors, university administrators, research integrity officers, junior faculty, and others attended the workshop. The aim of the workshop was to discuss how the implementation of RCR education can be used to inculcate ethical behavior and satisfy the National Science Foundation (NSF) and National Institutes of Health (NIH) requirements.

All NIH-funded trainees are expected to receive a minimum of

(See Workshop, page 4)

Is Your Data Safe When Someone Leaves Your Lab?

Joe Giffels, M.A.S., Asst. VP of Academic Affairs; Erin Golembewski, Ph.D., Sr. Assoc. Dean; and Alison Watkins, J.D., M.S., Research Compliance Officer, University of Maryland, Baltimore

As a Principal Investigator/Lab Director, you expect the researchers in your lab to handle the data that they use with care and to demonstrate scientific professionalism and integrity as they collaborate with you and your research team. In reality, lab personnel tend to come and go, and because expectations regarding data are not always communicated, they may not be met. The departure of a lab member presents potential risk to the integrity of your research data. The purpose of this article is to encourage the development and use of lab-specific policies and procedures for handling data when a member of the lab leaves.

Most departures are anticipated and represent positive transitions. Graduate students and postdoctoral fellows (postdocs) come to you for training and in the process participate in your lab's research. They are expected to be in your group for a finite period, during which time they have access to your existing research data and (ideally) contribute new data.

Though students and postdocs (and visiting scientists) are usually

(See Safe Data, page 5)

Scientific Digital Image Data: Handle With Care

Douglas W. Cromey, M.S., Southwest Environmental Health Science Center, University of Arizona

With the growing concern that scientific digital images used in grants and publications are not being manipulated correctly,[1-3] it is imperative that researchers be taught how to correctly work with digital images. At the University of Arizona, we have developed a twice-yearly, half-day workshop that introduces students, staff, and faculty to the basics of digital images.[4]

One point stressed throughout the workshop is that images are data. The digital images seen on our computers are pixels, a matrix of numbers, with positional and intensity information used to create each tiny dot on the screen. The fact that a pixel is a discrete element means that a digital image is only a representative sampling of the object being observed.

To begin, image data must be acquired correctly. This means one must understand the limitations of the instrument, the sample, and how the data will be used. The engineers and physicists building the instruments are aware of many of these limitations, but often the end users are not.

Correct acquisition also means that users should endeavor to avoid introducing their own biases into the process of sample selection and image acquisition. The samples should be telling the instrument operator what the results of the experiment are, not the other way around. Also, the operator should have a very good understanding of the range of variation found in the untreated appearance of the material being studied.

Once acquired, the digital image should be archived and redundantly backed up. We suggest that users incorporate the date (numeric MMDDYY) into the file or folder name. The date/time stamp of the file is frequently changed in the transfer between computers. The date is often the easiest way to locate that "needle in the haystack" image among the hundreds or thousands of images that some labs accumulate in the course of several years. The National Science Foundation (NSF) now mandates a well-documented data management plan in grant proposals.[5] It would not be surprising if the National Institutes of Health (NIH) follows suit in the future.

Files should also be archived in their original file format, and any image manipulations performed should always be done on a copy of the original image. If the original is in a proprietary format, it should be exported to a loss-less file format (TIF is recommended; JPG is not). The original data becomes the "gold standard" to which further image manipulations can be compared. In addition, if there is a question about the image manipulations performed, the original data can be produced to reassure journal editors and reviewers that the manipulations were appropriate.

Image manipulation creates changes in the underlying numbers in the image. Users should be able to produce a protocol or audit trail that shows what manipulations were performed, so that others can reproduce their work. Because the rules for appropriate image manipulation vary, users also should consult the journal's instructions to authors before manipulating images. General image manipulation guidelines[6,7] are also available for discussion and training.

Maintaining data integrity with scientific digital images is not difficult. However, given the ongoing problems with inappropriately handled image data, it is important for scientists to teach the members of their labs to be more careful in how they acquire, store, and manipulate this type of data.

Endnotes

1. Krueger, J., "Incidences of ORI cases involving falsified images." *Office of Research Integrity Newsletter,* 2009. 17(4): pp. 2-3.

2. Rossner, M., "How to guard against image fraud." *The Scientist,* 2006. 20(3): pp. 24.

3. Abraham, E., et al., "The ATS journals' policy on image manipulation." *Proc Am Thorac Soc,* 2008. 5(9): pp. 869.

4. Cromey, D.W., "Digital image ethics for a new generation." *Micros Today,* 2009. 17(5): pp. 72-73.

5. NSF, "Chapter II - Proposal Preparation Instructions: Data Management Plan." January 2011. Available at http://www.nsf.gov/pubs/policydocs/pappguide/nsf11001/gpg_2.jsp#dmp

6. Cromey, D.W., "Avoiding twisted pixels: Ethical guidelines for the appropriate use and manipulation of scientific digital images." *Sci Eng Ethics,* 2010. 16(4): pp. 639-667.

7. Vollmer, S.H., "Online Learning Tool for Research Integrity and Image Processing." 2008. Available at http://www.uab.edu/researchintegrityandimages/

Data Integrity Is Earned, Not Given

John S. Gardenier, D.B.A., Independent Science/Statistical Ethicist

The word *data* comes from the Latin plural of datum, originally meaning "something given."

It is also common to think of data as only the input to a research process and a small part of the total research effort. This paper urges an alternative mindset that considers the data to be the major consideration throughout the overall research effort. Data integrity is earned, not given. It is an essential component of the methodology and a primary (if not the primary) output to be communicated in any resulting presentations.

This discussion is limited to data integrity only in descriptive statistical analyses supporting scientific research. Although the argument applies to all fields of science, the most relevant here are the social sciences (including economics and biomedical research).

Data integrity must start from a context of a socially responsible research purpose. The research purpose determines what data are relevant and the needed amount, design, quality, and structure—as well as options for the methodology(ies). The study design dictates whether existing data are sufficient or specific data collection is needed. What were the key characteristics of the data in previous studies? How did they process their data to prepare it for the specific methodology applied? Did their conclusions follow logically from the data and analysis? Did they make their analytic data set available for replication? What lessons can be learned to improve the design at hand?

Whether the data to be used are already available or to be collected, the exact definitions and characteristics must be specified. The data must be consistent, implying strong data quality control. Their characteristics must be known in detail, perhaps from exploratory data analysis, so that all assumptions and needed caveats can also be identified. Special attention also must be paid to statistical sufficiency, such as power, and to confounding variables, missing data, and outliers. Any data omitted from the analysis must be meticulously justified.

Analytic methodology cannot be divorced from the data. Both must be specifically congruent in structure, relevance, and assumptions. Even more important than any measure of confidence or significance in the output is the logic that the conclusions follow from the data. Except as limited by factors beyond the scientists' control, the data should be made accessible. Multiple papers, reports, or presentations may be required to effectively present the study and results to different audiences. Within their technical capacity, each member of the audience should be able to understand the study and results fully and accurately and also have effective access to the data.

Scientists may mistakenly consider it an ethical obligation to accept data from colleagues or superiors for statistical analysis without detailed attention to all of the considerations above. That is incorrect. Without data integrity, it is impossible to achieve research integrity.

Reference

Panter, A.T., and Sterba, S.K. (Eds.). (2011). *Handbook of Ethics in Quantitative Methodology.* New York: Routledge.

Workshop in Response to NIH and NSF Requirements *(from page 1)*

eight hours of face-to-face training as part of these requirements.

Four panels were convened to discuss the implementation of RCR training. The panels highlighted the following topics: Perspectives from University Offices of Research on RCR Education; Collaboration Between Ethics Centers, Ethics Across Curriculum Programs, and University Offices of Research; Perspectives from Early Career Faculty on RCR Education; and Research Ethics Education in the Social Sciences.

Five themes emerged from the panel and small group discussions:

1. The need for setting goals and objectives for RCR education.

2. The value of both discipline-specific and interdisciplinary educational approaches.

3. The call for innovative strategies for teaching RCR.

4. The limitations of budget and resource constraints for the implementation of RCR education.

5. The need for greater awareness and proper utilization of online RCR educational resources. RCR resources available online include:

http://ori.hhs.gov

http://www.nationalethicscenter.net

http://research-ethics.net

http://scholarlyintegrity.org

One central belief expressed by members of the panel was the benefit of RCR training when presented as enhancing professional development rather than merely satisfying compliance requirements. Moreover, even though interdisciplinary education may be the most utilized method to deliver RCR education (because of limited time and resources), many participants also stated that having mentors share their experiences and best practices may be the best way to positively influence trainees. This approach is also consistent with the ideals articulated in the NIH policy on RCR training.

The RCREC will conduct another full-day workshop next year in Cincinnati as part of APPE's conference, March 1-4, 2012. The topic for next year's workshop is entitled "Models of Face-to-Face Research Integrity Education." A Call for Proposals will be sent to all RCREC members to elicit innovative and effective models of RCR instruction.

> "*One of the truest tests of integrity is its blunt refusal to be compromised.*"
>
> **Chinua Achebe**
> Nigerian Writer
> Nov. 16, 1930 - Present

Recent Studies in RCR

Bonito, A. J., Titus, S. L., Wright, D. E., "Assessing the Preparedness of Research Integrity Officers (RIOs) to Appropriately Handle Possible Research Misconduct Cases." Science and Engineering Ethics, DOI 10.1007, June 7, 2011, eprint.

Abstract: Institutions receiving federal funding for research from the U.S. Public Health Service need to have policies and procedures to both prevent research misconduct and adjudicate it when it occurs. The person who is designated to handle research misconduct is typically referred to as the Research Integrity Officer (RIO). In this interview study, we report on 79 RIOs who describe how they would handle allegations of research misconduct. Their responses were compared with those of two expert RIOs. The responses to the allegations in the scenarios demonstrated that RIOs are not uniformly well prepared to handle activities associated with reported allegations of research misconduct. We recommend greater preparation through directed training, use of check lists of possible behaviors necessary to consider when situations arise, being involved in a network of RIOs so that one can discuss options, and the possible need to certify RIOs.

Safe Data *(from page 1)*

involved with only a fraction of the total research data in your lab, research technicians and junior faculty often produce and access data that span multiple projects and longer time lines. The impact of such individuals' departures on the lab's research operations and data is usually significant.

Unfortunately, some researchers leave under less-than-favorable circumstances. Therefore, potential points of dispute should be raised before their departure. Risks of sabotage can be mitigated by securing the data as far in advance of a known departure as possible. Sudden, unanticipated departures present acute challenges best met by inventorying research data and materials to determine whether anything is missing or has been compromised and taking immediate and aggressive steps to remediate and prevent further loss.

To avoid jeopardizing the integrity of its research data, every lab should develop and be prepared to enforce policies and procedures governing the handling of data during the transition of a lab member out of the lab. The general tenets of such a policy may already be found in your lab's data handling policy. If they are, less disruption will occur when someone leaves the lab.

The needs and cultures of labs differ. Some policy points to consider include:

1. Raw data and research notebooks generally belong to the institution in which the lab resides and should remain in the lab.

2. A routine review of data can aid in the development of a culture of integrity in the lab.

3. Copies of all data (e.g., primary, compiled, and derived), research notebooks, and all analyses should be submitted for approval to the Lab Director (or a designee) well in advance (at least two weeks) of the known departure.

4. Plans to complete research and the disposition of all publications based on the data should be determined, as feasible, for all publications envisioned.

5. The disposition of all intellectual property emanating from the data should be determined (whenever possible) prior to departure.

6. A final meeting of the departing lab member and the Lab Director (including other lab members and collaborators) should be held shortly before the departure. At that exit interview, the departing lab member should physically turn over all raw data analyses and research notebooks.

7. All questions posed should be resolved, or a plan should be established for their resolution. It may also be advisable to produce and circulate written minutes of the meeting and have all present sign, attesting to the accuracy of the documentation.

8. The departing lab member should provide the Lab Director with forwarding contact information.

The importance of having policies and procedures on data handling in place when lab members depart cannot be overemphasized. These should be part of every lab's general data handling policies and procedures and should be communicated whenever personnel join the lab.

ORI thanks the following people for contributing articles to the newsletter:

Holly Bante

Douglas W. Cromey

James DuBois

John S. Gardenier

Joe Giffels

Erin Golembewski

Alison Watkins

Case Summaries

Junghee J. Shin, Ph.D.
New York Medical College

Based on the report of an investigation conducted by New York Medical College (NYMC) and additional analysis by the Office of Research Integrity (ORI) in its oversight review, the U.S. Public Health Service (PHS) found that Junghee J. Shin, Ph.D., former graduate student, NYMC, engaged in research misconduct in research supported by National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH), grants R01 AI048856 and R01 AI043063.

PHS found that the Respondent engaged in research misconduct by falsifying data in Figure 4 of a manuscript submitted to the journal *Infection and Immunity* (Shin, J.J., Godfrey, H.P., & Cabello, F.C. "Expression and localization of BmpC in *Borrelia burgdorferi* after growth under various environmental conditions." Submitted to *Infection and Immunity*; hereafter referred to as the "manuscript") and Figure 5 of a paper published in *Infection and Immunity* (Shin, J.J. Bryksin, A.V., Godfrey, H.P., & Cabello, F.C. "Localization of BmpA on the exposed outer membrane of *Borrelia burgdorferi* by monospecific anti-recombinant BmpA rabbit antibodies." *Infection and Immunity* 72(4):2280-2287, April 2004; hereafter referred to as the "paper." Retracted in: *Infection and Immunity* 76(10):4792, October 2008). Specifically, NYMC and ORI found that:

1. Dr. Shin falsified microscopic immunofluorescence blank images in Figure 4 of the manuscript (top row, 1st, 2nd, 4th, and 5th panels, and bottom row, 1st panel) and Figure 5 of the paper (top row, 1st and 5th panels, lower 1st panel) by using one blank image from an unknown experiment to falsely represent the preimmunization control conditions (intact cells and methanol fixation) as well as the negative staining of anti-BmpC and anti-FlaB in Figure 4 and anti-FlaB in Figure 5 on intact cells.

2. Dr. Shin falsified at least one of two images in Figure 4 of the manuscript and Figure 5 of the paper by using different portions of a green-red pair of microscopic immunofluorescence images (1230036.tif and 1230037.tif) because unfixed cells staining positive for BmpA in the top row, 4th panel, of Figure 5 were the same unfixed cells purportedly positive for OspA in the top row, 3rd panel, of Figure 4.

3. Dr. Shin falsified at least one of two images in Figure 4 of the manuscript and Figure 5 of the paper by using different photo cropping from a single microscopic immunofluorescence image (1230039.tif) to represent fixed cells positive for BmpA and labeled with anti-FlaB in the lower row, 5th panel, of Figure 5 and to also represent fixed cells positive for BmpC and stained with anti-FlaB in the lower row, 5th panel, of Figure 4.

Dr. Shin has entered into a Voluntary Settlement Agreement in which she has voluntarily agreed, for a period of three (3) years, beginning on April 5, 2011:

(1) that any institution that submits an application for PHS support for a research project on which the Respondent's participation is proposed or that uses her in any capacity on PHS-supported research, or that submits a report of PHS-funded research in which she is involved, must concurrently submit a plan for supervision of her duties to ORI for approval; the supervisory plan must be designed to ensure the scientific integrity of her research contribution; Respondent agrees that she will not participate in any PHS-supported research until such a supervision plan is submitted to ORI; and

(2) to exclude herself voluntarily from service in any advisory capacity to PHS, including but not limited to, service on any PHS advisory committee, board, and/or peer review committee, or as a consultant.

Vipul Bhrigu, Ph.D.
University of Michigan
Medical School

Based on the findings of an investigation by the University of Michigan Medical School (UMMS) and additional analysis conducted by the Office of Research Integrity (ORI) during its oversight review, ORI found that Vipul Bhrigu, Ph.D., former postdoctoral fellow, Department of Internal Medicine, UMMS, engaged in research misconduct in research funded by National Cancer Institute (NCI), National Institutes of Health (NIH), grant R01 CA098730-05.

Specifically, ORI found that the Respondent knowingly and intentionally tampered with research materials related to five (5) immunoprecipitation/Western blot experiments and switched the labels on four (4) cell culture dishes for cells used in the same type of experiments to cause false results to be reported in the research record. ORI also found that the Respondent tampered with laboratory research materials by adding ethanol to his colleague's cell culture media, with the deliberate intent to effectuate the death of growing cells, which caused false results to be reported in

Case Summaries *(continued)*

the research record. ORI has concluded that these acts seriously deviated from those that are commonly accepted within the scientific community for proposing, conducting, and/or reporting research.

ORI found that the Respondent's intentional tampering of his colleague's laboratory research constitutes research misconduct as defined by 42 CFR Part 93. ORI determined that the Respondent engaged in a pattern of dishonest conduct through the commission of multiple acts of data falsification. ORI also determined that the subterfuge in which he freely engaged for several months constitutes an aggravating factor. The Respondent attempted to mislead the University of Michigan (UM) police by initially denying involvement in the tampering and refusing to accept responsibility for this misconduct. The Respondent eventually made an admission only after the UM police informed him that his actions in the laboratory had been videotaped. This dishonest conduct established the Respondent's lack of present responsibility to be a steward of Federal funds (2 CFR § 376 *et seq.*; 42 CFR § 93.408).

The following administrative actions have been implemented for a period of three (3) years, beginning on April 7, 2011:

(1) Dr. Bhrigu is debarred from eligibility for any contracting or subcontracting with any agency of the United States Government and from eligibility for, or involvement in, nonprocurement programs of the United States Government, referred to as "covered transactions," pursuant to HHS' Implementation of OMB Guidelines to Agencies on Governmentwide Debarment and Suspension (2 CFR § 376 *et seq.*); and

(2) Dr. Bhrigu is prohibited from serving in any advisory capacity to the U.S. Public Health Service (PHS), including but not limited to, service on any PHS advisory committee, board, and/or peer review committee, or as a consultant.

Philippe Bois, Ph.D.
St. Jude Children's Research Hospital

Based on the findings of an investigation report by St. Jude Children's Research Hospital (St. Jude) and additional analysis conducted by ORI during its oversight review, ORI found that Philippe Bois, Ph.D., former postdoctoral fellow, Department of Biochemistry, St. Jude, engaged in misconduct in science and research misconduct in research funded by National Institute of General Medical Sciences (NIGMS), National Institutes of Health (NIH), grant R01 GM071596, and National Cancer Institute (NCI), NIH, grants P30 CA021765, P01 CA071907, R01 CA072996, and R01 CA100603.

ORI found that the Respondent knowingly and intentionally falsified data reported in two (2) papers:

1. Bois, P.R., Izeradjene, K., Houghton, P.J., Cleveland, J.L., Houghton, J.A., & Grosveld, C.G. "FOXO1a acts as a selective tumor suppressor in alveolar rhabdomyosarcoma." *J. Cell. Biol*. 170:903-912, September 2005 (hereafter referred to as "*JCB* 2005"); and

2. Bois, P.R., Borgon, R.A., Vornhein, C., & Izard, T. "Structural dynamics of alpha-actinin-vinculin interactions." *Mol. Cell. Biol*. 25:6112-6122, July 2005 (hereafter referred to as "*MCB* 2005").

Specifically, ORI found:

- Respondent committed misconduct in science and research misconduct by knowingly and intentionally falsely reporting in Figure 1A of *JCB* 2005 that FOXO1a was not expressed in cell lysates from alveolar rhabdomyosarcoma (ARMS) tumor biopsies, by selecting a specific FOXO1a immunoblot to show the desired result.
- Respondent engaged in misconduct in science and research misconduct by falsifying data presented in Figure 4B of *MCB* 2005 showing SDS-PAGE for papain digestion of VBS3 and alphaVBS, by falsely labeling lane 1 to represent papain only digestion, by falsely labeling lane 5 to represent papain digestion of the alphaVBS peptide, and by falsely inserting a band in lane 3 to represent the alphaVBS peptide.

ORI issued a charge letter enumerating the above findings of misconduct in science and proposing HHS administrative actions. Dr. Bois subsequently requested a hearing before an Administrative Law Judge (ALJ) of the Departmental Appeals Board (DAB) to dispute these findings. ORI moved to dismiss Dr. Bois' hearing request. On May 16, 2011, the ALJ of the DAB ruled in ORI's favor and dismissed Dr. Bois' hearing request. The ALJ found that Dr. Bois had not raised a genuine dispute over facts or law material to the findings of research misconduct and dismissed the hearing request pursuant to 42 CFR § 93.504(a)(2)(3).

Thus, the misconduct in science and research misconduct findings set forth

Case Summaries *(continued)*

above became effective, and the following administrative actions have been implemented for a period of three (3) years, beginning on May 26, 2011:

(1) Dr. Bois is debarred from eligibility for any contracting or subcontracting with any agency of the United States Government and from eligibility for, or involvement in, nonprocurement programs of the United States Government, referred to as "covered transactions," pursuant to HHS' Implementation of OMB Guidelines to Agencies on Governmentwide Debarment and Suspension (2 CFR § 376 *et seq.*); and

(2) Dr. Bois is prohibited from serving in any advisory capacity to the U.S. Public Health Service (PHS), including but not limited to, service on any PHS advisory committee, board, and/or peer review committee, or as a consultant.

"Knowing is not enough; we must apply. Willing is not enough; we must do."

Johann Wolfgang von Goethe
German Author
Aug. 28, 1749 - Mar. 22, 1832

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